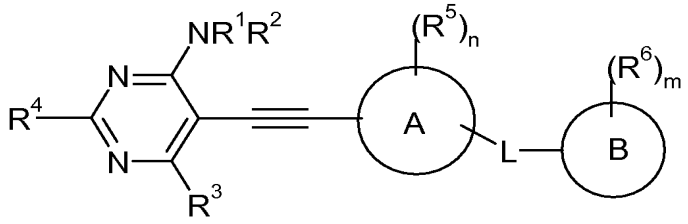
In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claims

1. (original): A compound of the Formula I:



Formula I

wherein:

R^1 and R^2 are independently selected from hydrogen, (1-6C)alkylsulfonyl, phenyl$(CH_2)_u$- wherein u is 0, 1, 2, 3, 4, 5 or 6, (1-6C)alkanoyl, (1-6C)alkyl, (1-6C)alkoxycarbonyl, (3-6C)cycloalkyl$(CH_2)_x$- in which x is 0, 1, 2, 3, 4, 5 or 6 , or a 5 or 6 membered heteroaryl ring, or **R^1 and R^2** together with the nitrogen atom to which they are attached represent a saturated or partially saturated 3 to 7 membered heterocyclic ring optionally containing another heteroatom selected from N or O;

wherein the (1-6C)alkyl, the (1-6C)alkanoyl and the (3-6C)cycloalkyl groups are optionally substituted by one or more groups independently selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy(1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, carbamoyl, mono(1-6C)alkylcarbamoyl, di-[(1-6C)alkyl]carbamoyl or–N(R^d)C(O)(1-6C)alkyl in which R^d is hydrogen or (1-6C)alkyl, or a saturated or partially saturated 3 to 7 membered heterocyclic ring, or a 5 or 6 membered heteroaryl ring,

wherein the (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy and (1-6C)alkoxy(1-6C)alkoxy(1-6C)alkoxy groups and the (1-6C)alkyl groups of the mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, mono(1-6C)alkylcarbamoyl, di-[(1-6C)alkyl]carbamoyl and/or -N(R^d)C(O)(1-6C)alkyl groups are optionally substituted by one or more hydroxy groups;

wherein the phenyl is optionally substituted by one or more groups independently selected from halo, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, wherein the (1-6C)alkyl and (1-6C)alkoxy groups are

optionally substituted by one or more groups independently selected from hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino;

and wherein any heterocyclic and heteroaryl rings within R^1 and/or R^2 are optionally independently substituted by one or more of the following: (1-4C)alkyl, (1-4C)alkoxy, (1-4C)alkoxy(1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, or a saturated or partially saturated 3 to 7 membered heterocyclic ring, or $-C(O)(CH_2)_zY$ wherein z is 0,1, 2 or 3 and Y is selected from hydrogen, hydroxy, (1-4C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

and provided that when R^1 and/or R^2 is a (1C)alkanoyl group, then the (1C)alkanoyl is not substituted by fluoro or hydroxy;

R^3 is selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy, (1-6C)alkoxy wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups selected from: fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, carbamoyl, mono(1-6C)alkylcarbamoyl or di-[(1-6C)alkyl]carbamoyl, amino, mono(1-6C)alkylamino or di(1-6C)alkylamino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, (1-4C)alkoxy,hydroxy, amino, mono(1-6C)alkylamino or di(1-6C)alkylamino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

or **R^3** represents a group **$-NR^1R^2$** as defined above;

R^4 is selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy;

A represents an aryl group or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl;

R^5 is selected from cyclopropyl, cyano, halo, (1-6C)alkoxy or (1-6C)alkyl, wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by cyano or by one or more fluoro;

n is 0, 1, 2 or 3;

L is attached meta or para on ring A with respect to the point of attachment of the ethynyl group and represents -C(R^aR^b)C(O)N(R^9)-, -N(R^8)C(O)C(R^aR^b)-, -N(R^8)C(O)N(R^9)-, -N(R^8)C(O) O-, or –OC(O) –N(R^9)-, wherein R^8 and R^9 independently represent hydrogen or (1-6C)alkyl and wherein R^a and R^b independently represent hydrogen or (1-6C)alkyl or R^a and R^b together with the carbon atom to which they are attached represent (3-6C)cycloalkyl ;

B represents a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring, an aryl group, a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl, or a 8, 9 or 10 membered bicyclic group which optionally contains 1, 2, 3 or 4 heteroatoms independently selected from N, O and S and which is saturated, partially saturated or aromatic;

R^6 is selected from halo, cyano, oxo, a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring -$S(O)_p$-(1-6C)alkyl wherein p is 0, 1 or 2, -N(R^a)C(O)(1-6C)alkyl in which R^a is hydrogen or (1-6C)alkyl; or

R^6 is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the (1-6C)alkyl, -$S(O)_p$-(1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, a (3-7C)cycloalkyl ring or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

wherein the (3-7C)cycloalkyl ring and saturated or partially saturated 3 to 7 membered heterocyclic ring are optionally independently substituted by one or more groups selected from (1-6C)alkyl; and

m is 0, 1, 2 or 3;

and when B is a (3-7C)cycloalkyl ring or a saturated or partially saturated 3 to 7 membered heterocyclic ring or a saturated or partially saturated 8, 9 or 10 membered bicyclic group, the rings and bicyclic group optionally bear 1 or 2 oxo or thioxo substituents;

and salts thereof.

2. (original): A compound of Formula I according to Claim 1, wherein:

R^6 is selected from halo, cyano, a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or an alkanoylamino group -N(R^c)C(O)(1-6C)alkyl in which R^c is hydrogen or (1-6C)alkyl; or

R^6 is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, a (3-7C)cycloalkyl ring or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

and salts thereof.

3. (original): A compound of the Formula I according to claim 1, wherein

R^1 and R^2 are independently selected from hydrogen, (1-6C)alkylsulfonyl, phenyl$(CH_2)_u$- wherein u is 0, 1, 2, 3, 4, 5 or 6, (1-6C)alkanoyl, (1-6C)alkyl, (1-6C)alkoxycarbonyl, or (3-6C)cycloalkyl$(CH_2)_x$- in which x is 0, 1, 2, 3, 4, 5 or 6, or **R^1 and R^2** together with the nitrogen atom to which they are attached represent a saturated or partially saturated 3 to 7 membered heterocyclic ring optionally containing another heteroatom selected from N or O;

wherein the alkyl and the cycloalkyl groups are optionally substituted by one or more groups selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

and wherein the phenyl is optionally substituted by one or more groups selected from halo, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, wherein the (1-6C)alkyl or (1-6C)alkoxy are optionally substituted by hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino;

R^3 is selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy, wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or

di-[(1-6C)alkyl]amino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

or $\mathbf{R^3}$ represents a group $\mathbf{-NR^1R^2}$ as defined above;

$\mathbf{R^4}$ is selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy;

A represents an aryl group or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl;

$\mathbf{R^5}$ is selected from cyano, halo, (1-6C)alkoxy or (1-6C)alkyl optionally substituted by cyano or by one or more fluoro;

n is 0, 1, 2 or 3;

L is attached meta or para on ring A with respect to the point of attachment of the ethynyl group and represents $-C(R^aR^b)C(O)N(R^9)-$, $-N(R^8)C(O)C(R^aR^b)-$, $-N(R^8)C(O)N(R^9)-$, $-N(R^8)C(O)O-$, or $-OC(O)N(R^9)-$, wherein R^8 and R^9 independently represent hydrogen or (1-6C)alkyl and wherein R^a and R^b independently represent hydrogen or (1-6C)alkyl or R^a and R^b together with the carbon atom to which they are attached represent (3-6C)cycloalkyl;

B represents a (3-7C)cycloalkyl ring, an aryl group or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl;

$\mathbf{R^6}$ is selected from halo, cyano, a saturated or partially saturated 3 to 7 membered heterocyclic ring or an alkanoylamino group $-N(R^a)C(O)$(1-6C)alkyl in which R^a is hydrogen or (1-6C)alkyl; or $\mathbf{R^6}$ is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups

selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, or a saturated or partially saturated 3 to 7 membered heterocyclic ring; and

m is 0, 1, 2 or 3;

and when m is at least 2 then two substituents on adjacent carbon atoms in ring B may together represent a methylenedioxy group;

and salts thereof.

4. (currently amended): A compound according to ~~any one of~~ Claims 1~~, 2 and 3~~ wherein A is selected from phenyl, pyridyl, thiazolyl, thiadiazolyl or pyrimidinyl.

5. (currently amended): A compound according~~ly~~ to ~~any one of the preceding~~ claim~~s~~ 1 wherein B is selected from phenyl, 2,3-di-hydro-indenyl, piperidinyl, pyridyl, pyrazolyl, isothiazolyl, thiadiazolyl, isoxazolyl, benzodioxinyl, benzodioxolyl or tetrahydropyranyl

6. (currently amended): A compound according~~ly~~ to ~~any one of the preceding~~ claim~~s~~ 1 wherein L is selected from $-N(R^8)C(O)N(R^9)-$, $-N(R^8)C(O)O-$ or $-N(R^8)C(O)CH_2-$ wherein R^8 and R^9 independently represent hydrogen or (1-6C)alkyl.

7. (currently amended): A compound according~~ly~~ to ~~any one of the preceding~~ claim~~s~~ 1 wherein R^1 and R^2 are both hydrogen or R^1 is hydrogen or (1-6C)alkyl and R^2 is (1-6C)alkyl

wherein (1-6Calkyl) is optionally substituted by hydroxy, amino, mono(1-6C)alkylamino or di(1-6C)alkylamino, carbamoyl, (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, $-N(R^d)C(O)$(1-6C)alkyl in which R^d is hydrogen or (1-6C)alkyl, aryl (particularily phenyl), a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring;

wherein the (1-6C)alkoxy, mono(1-6C)alkylamino and $-N(R^d)C(O)$(1-6C)alkyl groups are optionally substituted by hydroxy; and

wherein an aryl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring is optionally substituted by (1-4C)alkyl, (1-4C)alkoxy or $-C(O)CH_2Y$ wherein Y is selected from hydroxy or di(1-6C)alkylamino.

8. (currently amended): A compound accordingly to ~~any one of the preceding~~ claims 1 wherein R^3 and R^4 are both hydrogen.

9. (currently amended): A compound accordingly to ~~any one of the preceding~~ claims 1 wherein R^6 is independently selected from halo, cyano, oxo, (3-7C)cycloalkyl, a saturated 3 to 7 membered heterocyclic ring (optionally substituted by (1-4C)alkyl), -N(R^c)C(O)(1-6C)alkyl wherein R^c is hydrogen or (1-6C)alkyl (particularily (1-4C)alkyl), (1-6C)alkyl (optionally substituted by halo) or (1-6C)alkoxy and m is selected from 1 or 2.

10. (original): A compound according to Claim 1 which is any one or more of examples 1 to 51 or a salt thereof.

11. (currently amended): A pharmaceutical composition which comprises a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in ~~any one of~~ claims 1 ~~to 10~~ in association with a pharmaceutically acceptable diluent or carrier.

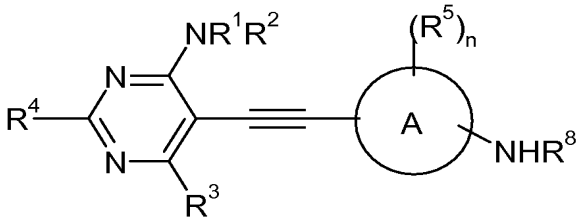
12. (canceled)

13. (canceled)

14. (canceled)

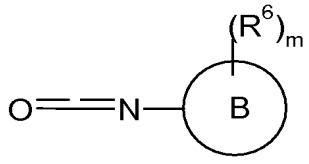
15. (original): A process for preparing a compound of formula I, as defined in Claim 1, or a pharmaceutically acceptable salt thereof (wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} L , ring A and ring B, n and m are, unless otherwise specified, as defined in Claim 1) comprising:

(a) For compounds of the formula I wherein L is -N(R^8)C(O)N(H)-, the reaction of a compound of the formula II:



II

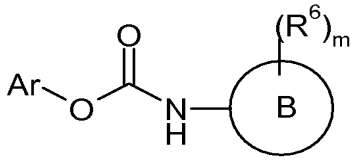
wherein R^1, R^2, R^3, R^4, R^5, R^8, n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an isocyanate of the formula IV:



IV

wherein R^6, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

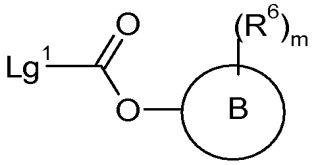
(b) For compounds of the formula I wherein L is $-N(R^8)C(O)N(H)-$, the reaction of a compound of the formula II as defined above with an aryl carbamate of the formula III:



III

wherein Ar is a suitable aryl group, for example phenyl, and R^6, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

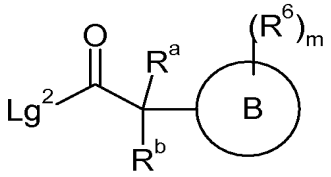
(c) For compounds of the formula I wherein L is $N(R^8)C(O)-O-$, the reaction of a compound of the formula II as defined above with a compound of the formula XI:



XI

wherein Lg^1 is a suitable displaceable group for example halogeno (such as fluoro, chloro or bromo) and R^6, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

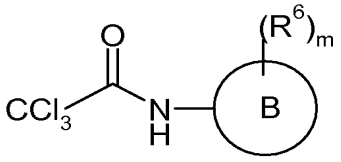
(d) For compounds of the formula I wherein L is $N(R^8)C(O)C(R^aR^b)$, the reaction of a compound of the formula II as defined above with a compound of the formula IX:



IX

wherein Lg^2 is a suitable displaceable group for example hydroxy, halogeno (such as fluoro, chloro or bromo), R^x-C(O)-O- or R^x-O- (wherein R^x is a suitable alkyl or aryl group) and R^6, R^a, R^b, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

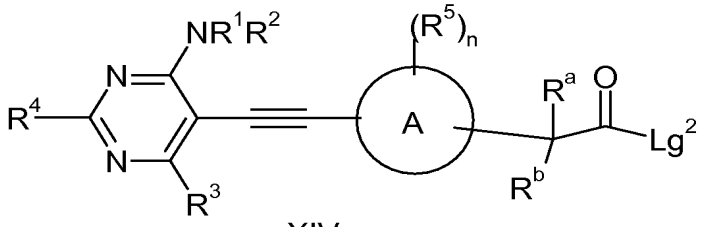
(e) For compounds of the formula I wherein L is -N(R^8)C(O)N(H)-, the reaction of a compound of the formula II as defined above with a trichloroacetylamine of the formula XIII:



XIII

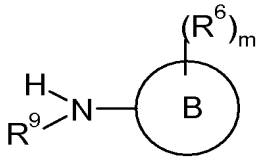
wherein R^6, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

(f) For compounds of the formula I wherein L is -C(R^aR^b)C(O)N(R^9)-, the reaction of a compound of the formula XIV:



XIV

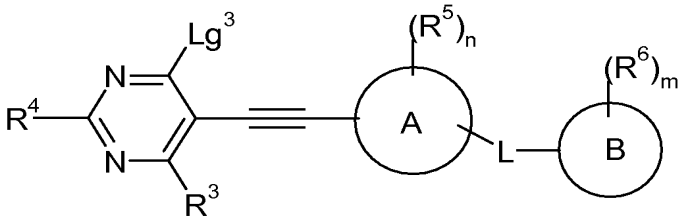
wherein Lg^2 is a suitable displaceable group as described above and R^1, R^2, R^3, R^4, R^5, R^a, R^b, n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV:



XV

wherein R^6, R^9, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

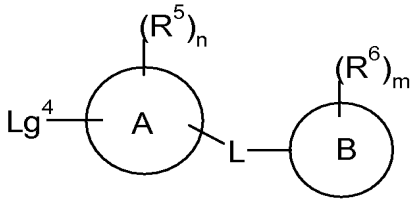
(g) The reaction of a compound of the formula XVI:



XVI

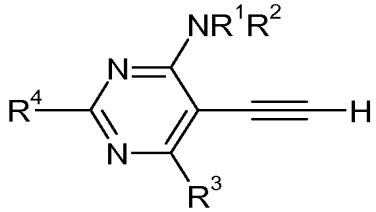
wherein Lg^3 is a suitable displaceable group for example halogeno (such as fluoro, chloro, bromo or iodo), methyl sulfonyl, methylthio or aryloxy (such as phenoxy) and R^3, R^4, R^5, R^6, n, m, A, B and L have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula HNR^1R^2, wherein R^1 and R^2 have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

(h) The reaction of a compound of the formula XVII:



XVII

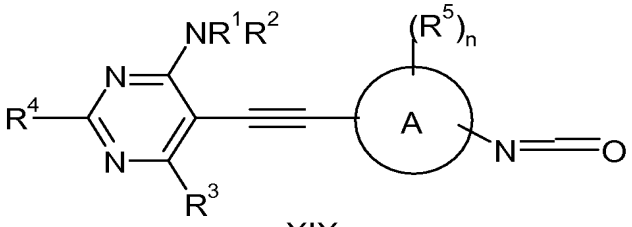
wherein Lg^4 is a suitable displaceable group for example halogeno (such as chloro, bromo or iodo) or a sulfonyloxy group (such as trifluoromethylsulfonyloxy) and R^5, R^6, n, m, A, B and L have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an alkyne of the formula XVIII:



XVIII

wherein R^1, R^2, R^3 and R^4 have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

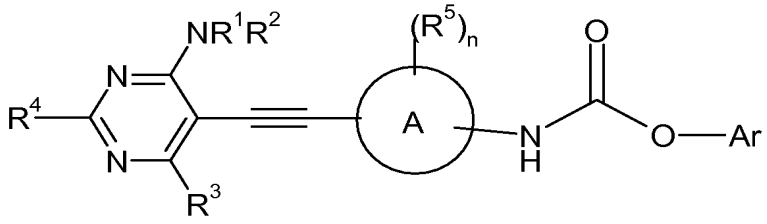
(i) For compounds of the formula I wherein L is -N(H)C(O)N(R^9)-, the reaction of an isocyanate of the formula XIX:



XIX

wherein R^1, R^2, R^3, R^4, R^5, n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV as defined above; or

(j) For compounds of the formula I wherein L is -N(H)C(O)N(R^9)-, the reaction of a compound of the formula XX:



XX

wherein Ar is a suitable aryl group, for example phenyl, and R^1, R^2, R^3, R^4, R^5, n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV as defined above.

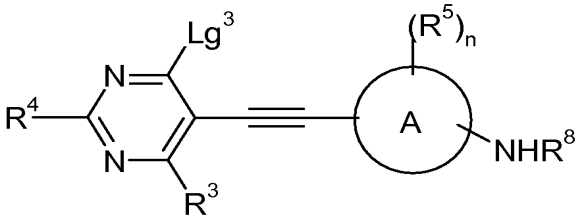
and thereafter if necessary:

i) converting a compound of the Formula (I) into another compound of the Formula (I);

ii) removing any protecting groups;

iii) forming a salt.

16. (currently amended): A compound selected from Formulae II, XIV, XVI, XIX and ~~-~~XX as defined in Claim 15 or a compound of Formula VIc:



VIc

or salt thereof, wherein ~~Lg3~~Lg^3, R^3, R^4, R^5 and n are as defined in Claim 15.

17. (new): A method of inhibiting Tie2 receptor tyrosine kinase in a warm-blooded animal in need of such treatment, which comprises administering to said animal an effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, according to claim 1.

18. (new): A method for producing an anti-angiogenic effect in a warm-blooded animal in need of such treatment, which comprises administering to said animal an effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, as claimed in claim 1.